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EXAMINER	
MAKAR, KIMBERLY A	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/772,502	ROZEMA ET AL.	
	Examiner	Art Unit	
	Kimberly A. Makar, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-17,19,20 and 22-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-17,19,20 and 22-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 2/5/04 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/19/07 has been entered.

Claim Objections

2. Claim 13 is objected to because of the following informalities: claim 13 is not grammatically correct. Claim 13 is missing an article in the phrase "delivery of polynucleotide". The phrase should read "delivery of a polynucleotide". Claim 13 also uses the incorrect article in the phrase "and a amphiphilic membrane active polyvinylether" and should read, "and an amphiphilic membrane active polyvinylether." Appropriate correction is required.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 13, 16-17 and 22-24 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11-13, and 18-21 of U.S. Patent No. 7,098,032 (of record 12/18/06). Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). The MPEP states, at §804, that:

21. [t]he specification can always be used as a dictionary to learn the meaning of a term in the patent claim. *In re Boylan*, 392 F.2d 1017, 157 USPQ 370 (CCPA 1968). Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970).

5. The court in *Vogel* recognized "that it is most difficult, if not meaningless, to try to say what is or is not an obvious variation of a claim," but that one can judge whether or not the invention claimed in an application is an obvious variation of an embodiment disclosed in the patent which provides support for the patent claim. According to the court one must first "determine how much of the patent disclosure pertains to the invention claimed in the patent" because only "[t]his portion of the specification supports

the patent claims and may be considered." The court pointed out that "this use of the disclosure is not in contravention of the cases forbidding its use as prior art, nor is it applying the patent as a reference under 35 U.S.C. 103, since only the disclosure of the invention claimed in the patent may be examined."

6. US Patent 7,098,032 teaches amphiphilic polymers (column 20, lines 64- column 21) and "Membrane Active" compounds (column 21, 12-31). Additionally, claims 11-13, 18-21 deal with the making an amphipathic copolymer comprising a polycation and a polyanions. Example 2 of Patent 7,098,032 uses a polyvinyl ether to produce polycations, which are used in the amphiphilic copolymers of patented claim 11. Additionally, examples 5-6 of Patent 7,098,032 teach the formation of pH-labile polyampholytes using CDM thioesters and cysteine-modified polycations, and the formation of polymer and DNA complexes in the presence of CDM modified polymers in the presence of HEPES, which are the same steps of preparation that produces the amphiphilic polymers of the instant specification (see page 17 line 22 through page 18 line 27; and page 20). Thus the polymers produced in the patent are inherently amphiphilic, in addition to being polyampholytes.

7. Thus is would have been obvious to modify the claims of Patent 7,098,032 to amphiphilic polymers as the specific embodiments of Patent 7,098032 teach the production of ampholytic, amphiphilic polymers. The double patenting rejection is maintained for reasons stated in the office action dated 12/18/06 and expanded herein.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 13-17, 19-20, 22 and 25-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Meier et al (US Patent No: 6,616,946) of record 12/18/06. Claims 13-17, 19-20, 22 and 25-30 recite a composition for the delivery of a polynucleotide to a cell comprising the polynucleotide and an amphiphilic membrane active polyvinylether. The composition is further limited wherein the polynucleotide is bound with the polyvinylether via and electrostatic interaction, a covalent linkage, or a labile covalent linkage. The composition is further limited wherein the polyvinyl ether consists of a cationic polyvinylether. The composition further comprises a maleic anhydride modified polyvinylether and wherein the modified polyvinylether consists of an anionic polyvinylether. The composition is further limited wherein the polynucleotide is selected from the list consisting of: DNA, plasmid DNA, linear DNA, double stranded DNA, single stranded DNA, RNA, an expression cassette, antisense oligonucleotide, siRNA, microRNA, RNA expression cassette, ribozyme, dsRNA, and synthetic polynucleotides or wherein the polynucleotide inhibits the expression of a gene in the cell. The composition is further limited wherein the polyvinylether consists of a modified

polyvinylether and wherein the modified polyvinyl ether consists of an anionic polyvinylether, and an amphiphilic polyvinylether. The composition is further limited wherein the modification consists of a reversible modification and therein the polynucleotide is covalently linked to the polyvinyl ether.

10. This rejection is maintained from the original rejection dated 12/18/06 and modified to address limitations added 2/26/07.

11. The specification fails to define "modified polyvinylether" in clear concise terms. In reading the specification, it appears that "modified polyvinylether" refers to a polyvinylether that has had functional groups added to the copolymer.

12. The specification fails to define "labile covalent linkage" in specific terms. In reading the specification, it appears that "labile covalent linkage" refers to covalent bonds that are reversible.

13. The specification fails to define "reversible modification". In reading the specification, it appears that "reversible modification" refers to the ability to remove the added functional groups.

14. The specification teaches, "[a]ntisense therapies hold tremendous promise for treating a wide variety of human diseases. These therapies are based on the selective inhibition of expression of a specific gene. Because they are highly specific, antisense agents could in theory have fewer side effects and display less toxicity than traditional drugs. In addition, because antisense agents exert their effects by binding to a complementary sequence in a target RNA molecule, designing antisense agents to specifically inhibit a particular RNA species is straightforward." (Page 16, lines 11-18).

15. Meier et al (US Patent No: 6,616,946) teaches a stimulus responsive hollow particle comprising copolymers (see abstract). Specifically Meier teaches that the copolymers comprise amphiphilic hydrophobic polyvinylether (column 9, lines 28-39) and amphiphilic hydrophilic polyvinylether (column 10, lines 6-13). Meier teaches these hollow polyvinylether copolymers further comprise biological agents, such as proteins, nucleic acids, and antisense oligonucleotides (column 15, lines 14-37). Since Meier teaches the transfer of antisense oligonucleotides into cells, and the specification details how antisense technology is used to inhibit gene expression in a cell, Meier teaches the polynucleotide inhibits expression of a gene in a cell. Meier teaches that the interaction between the agent and the polyvinylether is ionic (electrostatic) (column 18, lines 28-32) or through covalent bonds (column 18, lines 34-36).

16. Furthermore, Meier teaches that the polymers used in the hollow particles can be modified with a positive (cationic) or negative (ionic) charge (column 16, lines 43-45). Meier also teaches that the copolymers can be modified by the addition of maleic acid which renders the copolymers pH sensitive (column 6, lines 5-37). Meier teaches that the modified polyvinylether copolymers are rendered anionic with changes in pH (column 6, lines 5-37, particularly lines 29-31). Meier teaches that the formation of the hollow particles is a "result of the amphiphilic nature of the copolymers. The aggregation of the non-crosslinked particles occurs via non-covalent interactions and therefore is reversible" (column 8, lines 57-60). Additionally, Meier teaches that the hollow particles comprise degradable bonds (column 11, lines 37-46) and that "[degradable links or regions can be incorporated into the responsive polymer, or

elsewhere into the structure of the hollow particles, so that the particles degrade over a period of time, such as after release of the active agent at the desired location" (column 16, lines 62-66). Since Meier teaches that the polynucleotides can be covalently linked to the core polyvinylether, he teaches that the bond can thus be a degradable (labile covalent) bond.

17. Meier also teaches that these copolymer particles are expressly made for nucleotides and drug delivery as an advance over liposomes (column 1, lines 10-60). He also states that these particles are modified to comprise targeting molecules, such as antibodies and ligands, and that "antibodies may be directed to specific cell surface molecules or antigens expressed when a cell type becomes diseased, for example a cancer" (column 15, lines 50-64). An inherent property of these amphipathic particles would be the ability to alter membrane structure, through the attachment of the antibodies to the cell membrane, but also as delivery vehicles which fuse to the cells for delivery purposes, as replacements for liposomes.

18. Thus Meier teaches an amphiphilic membrane active polyvinylether/polynucleotide composition wherein the polyvinylethers are ionic, cationic or anionic, and are reversibly modified by a maleic anhydride. Meier further teaches that the interaction between the polynucleotide is ionic, covalent or labile covalent. Thus Meier teaches the claimed invention.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claim 23-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meier et al (US Patent No: 6,616,946) in view of Merdan et al (Prospects for cationic polymers in gene and oligonucleotide therapy against cancer, Advanced Drug Delivery Reviews, 2002. 54:715-758) of record 12/18/06. Claims 23-24 recite a composition for the delivery of a polynucleotide to a cell comprising the polynucleotide and a membrane active polyvinylether wherein the polynucleotide expresses a protein or wherein the polynucleotide expresses an RNA.

21. Meier et al (US Patent No: 6,616,946) teaches a composition comprising a polynucleotide and a membrane active amphiphilic polyvinylether (see above). Meier does not teach that the polynucleotide expresses a protein, nor that the polynucleotide expresses an RNA.

22. Merdan et al (Prospects for cationic polymers in gene and oligonucleotide therapy against cancer, Advanced Drug Delivery Reviews, 2002. 54:715-758) teaches gene therapy utilizing cationic polymers are viable ways with tremendous potential for treating cancer (see abstract). Merdan teaches that strategies for cancer gene therapy treatments include the "manipulation of gene expression either on the transcriptional or

on the translation level" and "a deficient gene can either be replaced or the effect of an unwanted gene can be blocked" (page 717, Column I, Introduction Section). Merdan teaches that polycations are able to complex with polynucleotides such as DNA plasmids, antisense oligonucleotides and RNA (see figures 1 and 4). Merdan teaches that the vector/nucleic acid complex is delivered to the target tissue, where it is taken into the cell for further processing (page 722, column I, section 3). Once inside the cell the DNA or RNA component of the polyplexes has to reach the site of action in the cell (page 735, section 3.2.5). Merdan teaches that the plasmid DNA "has to be transported into the nucleus, on order to exhibit the desired gene expression" but that ribozymes and RNA may function in the cytosol (page 735, section 3.2.5). Merdan further teaches that ribozymes are "RNA molecules endowed with catalytic cleaving mRNA molecules in a sequence specific, catalytic manner" (page 740, section 4.1.2).

23. A skilled artisan would have been motivated to combine the teaching of Meier on a composition comprising a polynucleotide and a polyvinylether with the teaching of Merdan on the benefits of using polycation/polynucleotide complexes for the treatment of cancer where the polynucleotide expresses a gene or an RNA because alteration of gene expression, either through up-regulation of a deficient gene by translation of the plasmid DNA into protein or down regulation of a gene through the expression of a ribozyme are both viable strategies for gene therapy. It would have been obvious to the skilled artisan to combine the teaching of Meier on a composition comprising a polynucleotide and a polyvinylether with the teaching of Merdan on the benefits of using polycation/polynucleotide complexes for the treatment of cancer where the

polynucleotide expresses a protein or an RNA because the ultimate goal of gene therapy is the alteration of endogenous protein levels- either through the addition of a deficient gene or protein, or the suppression of an overabundant gene or protein- thus by expressing the protein or the RNA are obvious limitations for the composition of the instant invention. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention.

Response to Arguments

24. Applicant's arguments filed 09/19/07 have been fully considered but they are not persuasive. In their response applicants traverse the Double Patenting rejection of claims 13-30 over US Patent 7,098,032. Applicants argue that the claims of Patent 7,098,032 are directed towards polyampholyte polymers, not amphiphilic polymers. This argument is not persuasive. The claims of US Patent 7,098,032 are indeed directed towards polyampholytes, and not amphiphilic polymers. However, the specification of Patent 7,098,032 teaches specific embodiments which are inherently amphiphilic, and are produced using that same methodology that are used to produce the amphiphilic polymers of the instant invention. Therefore, it would have been obvious to the skilled artisan to modify the claims of Patent 7,098,032 to include amphiphilic polymers. Thus this rejection is maintained for reasons of record and repeated herein.

25. In their response, applicant's traverse the 102(e) rejection of claims 13-22 and 25-30 as being taught by Meier et al (US Patent 6,616,946). Applicant's argue that the antibodies of the polymer complexes taught by Meier et al do not define membrane activity as defined by the applicant's specification, and that one skilled in the art would not consider an antibody to possess any of the membrane activities as asserted by an accompanying 1.132 Declaration. Additionally, applicants assert that the hollow spheres comprising polymers that are taught in the Meier patent possess the membrane fusion characteristics inherent with some, but not all liposomes, and that the term fuse and fusion are not present in the Meier patent, but that nowhere in the patent is it suggested that the particle possess any ability to directly affect transfer of the agent into the cell. Applicants assert Meier describes the use of their particle to release an agent in a region of a human body, but makes no claim or suggestion of any ability to deliver the agent into a cell.

26. Applicant's arguments are respectfully not persuasive. In response to applicant's assertion that the targeting antibodies of Meier do not possess membrane activity as defined in the specification, the Examiner disagrees. The instant specification defines membrane activity as:

27. Membrane active - Membrane active polymers or compounds are molecules that are able to alter membrane structure. This change in structure ***can*** be shown by the compound inducing one or more of the following effects upon a membrane: an alteration that allows small molecule permeability, pore formation in the membrane, a fusion and/or fission of membranes, an alteration that allows large molecule permeability, or a dissolving of the membrane. This alteration ***can*** be functionally defined by the compound's activity in at least one the following assays: red blood cell lysis (hemolysis), liposome leakage, liposome fusion, cell fusion, cell lysis and endosomal release. More specifically membrane active compounds allow for the transport of molecules with

molecular weight greater than 50 atomic mass units to cross a membrane. This transport ***may*** be accomplished by either the total loss of membrane structure, the formation of holes (or pores) in the membrane structure, or the assisted transport of compound through the membrane. (page 9 of the instant specification; emphasis added).

28. Applicants assertion that "the alteration of membrane structure must induce either small molecule permeability, pore formation in the membrane, a fusion and or fission of membranes, an alteration that allows large molecule permeability, or a dissolving of the membranes; which can be shown by red blood cell lysis (hemolysis), liposome leakage, liposome fusion, cell fusion cell lysis or endosome release" (page 4 of applicant's response) are only ways which "can" show membrane activity, and is in no way an absolute requirement of the specification, nor the instant claims.

29. Additionally, applicants arguments that Meier polymers make no claim or suggestion of any ability to deliver the agent to a cell is not persuasive. First, the instant claims are directed to "a composition for delivery of a polynucleotide ***to*** a cell" and not "a composition for delivery of a polynucleotide ***into*** a cell" (emphasis added) as applicants are appearing to argue. Thus there is no requirement in the instant claims that the polynucleotide is delivered into the cell. In response to applicant's arguments that Meier et al only teaches specific delivery to different regions of the body and not to individual cell is not persuasive. Meier et al teaches modification of the polymer spheres can include specifically targeting hepatocytes, which reads on targeted delivery to a cell:

30. Additionally, the surface of polymeric hollow particles can easily be modified with specific ligands. This can be achieved, for example, by copolymerization with a small fraction of ligand-bearing comonomers, e.g. galactosyl-monomers. It is well known that

such polymer-bound galactosyl-groups are recognized by the receptors at the surface of hepatocytes (Weigel, et al. J. Biol. Chem. 1979, 254, 10830). Such labeled particles can be administered to a patient where they will migrate to and bind to the target (column 4, lines 18-26 of Meier et al).

31. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., fusion/fuse or ability to deliver the agent *into* a cell) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

32. Finally, the instant claims are directed towards a composition, and not a method. Thus any composition comprising the properties of the instant claims, either explicitly or implicitly, also reads on the claimed invention. The hollow polymer spheres of Meier et al do indeed teach all of the claimed invention, and thus claims 13-17, 19-20, 22, 25-30 are properly rejected under 102(e). Thus this rejection is maintained for reasons of record and repeated herein.

33. Applicant's traverse the 103(a) rejection of claims 23-24 as being obvious over Meier et el in view of Merdan et al. Applicants argue that the arguments presented in view of Meier et al are sufficient to obviate the 103(a) rejection. Applicants present no arguments against Merdan et al.

34. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208

USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

35. Additionally, the examiner has addressed applicant's arguments regarding Meier et al, and is not persuaded by such arguments. Thus claims 23-24 remain rejected under 103(a).

36. The declarations under 37 CFR 1.132 filed 09/19/07 are insufficient to overcome the rejection of claims 13-22 and 25-30 as being taught by Meier et al (US Patent 6,616,946) as set forth in the last Office action because:

37. In the 1.132 declaration provided by Dr. Zane Neal is not persuasive. In his declaration, Dr. Neal states "antibodies, as used in 6,616,946, would not be considered to posess membrane activity as defined the 11/06/2000". It is unclear to what Dr. Zane is referring to. Additionally, it has already been made of record in this response, how "membrane activity" is not defined in the specification more than "Membrane active polymers or compounds are molecules that are able to alter membrane structure" and that any functional test suggested by the instant specification is only a possible measure of testing membrane activity, and not limiting, nor defining.

38. Additionally, the 1.132 declaration provided by Dr. Sean Monahan is not persuasive. In his declaration, Dr. Monahan states that he is an author on the Meier et al patent 6,616,949, and he states, "while there hollow particles appear to be able to release their contents in response to a specific stimuli, such as pH, there is no indication they contemplate delivery to a target site within the cell. The inventions of US Patent

6,616,946 do no describe or suggest any property of the hollow spheres that would enable them to disrupt a cellular membrane" (page 2 of Dr. Monahan's declaration).

39. Dr. Monahan's arguments are not persuasive. First, as already shown above, the instant claims recite a composition capable to delivery of a polynucleotide "to a cell" and not "into a cell". Secondly, there is no requirement in the instant claims that the polymers are required "to contemplate delivery to a target site within the cell." Thirdly, as stated above, Meier et al specifically and explicitly teaches that ligands can be used to target the polymers to specific cells, not necessarily only regions of the body (see above). And finally, the instant specification does not limit "membrane active" to the disruption of the cell membrane, only "membrane active polymers or compounds are molecules that are able to alter membrane structure." Thus Dr. Neal and Monahan's arguments are not persuasive.

Conclusion

40. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Makar, Ph.D. whose telephone number is 571-272-4139. The examiner can normally be reached on 8AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D. can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kam/11/25/07

Joe Woitach
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